LUGANO Phase 3 Trial of Bioerodible EYP-1901 (vorolanib intravitreal insert) vs Aflibercept in Patients with Neovascular Age-Related Macular Degeneration: FIRST-TIME VISION AND ANATOMIC OUTCOMES

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Study disclosures

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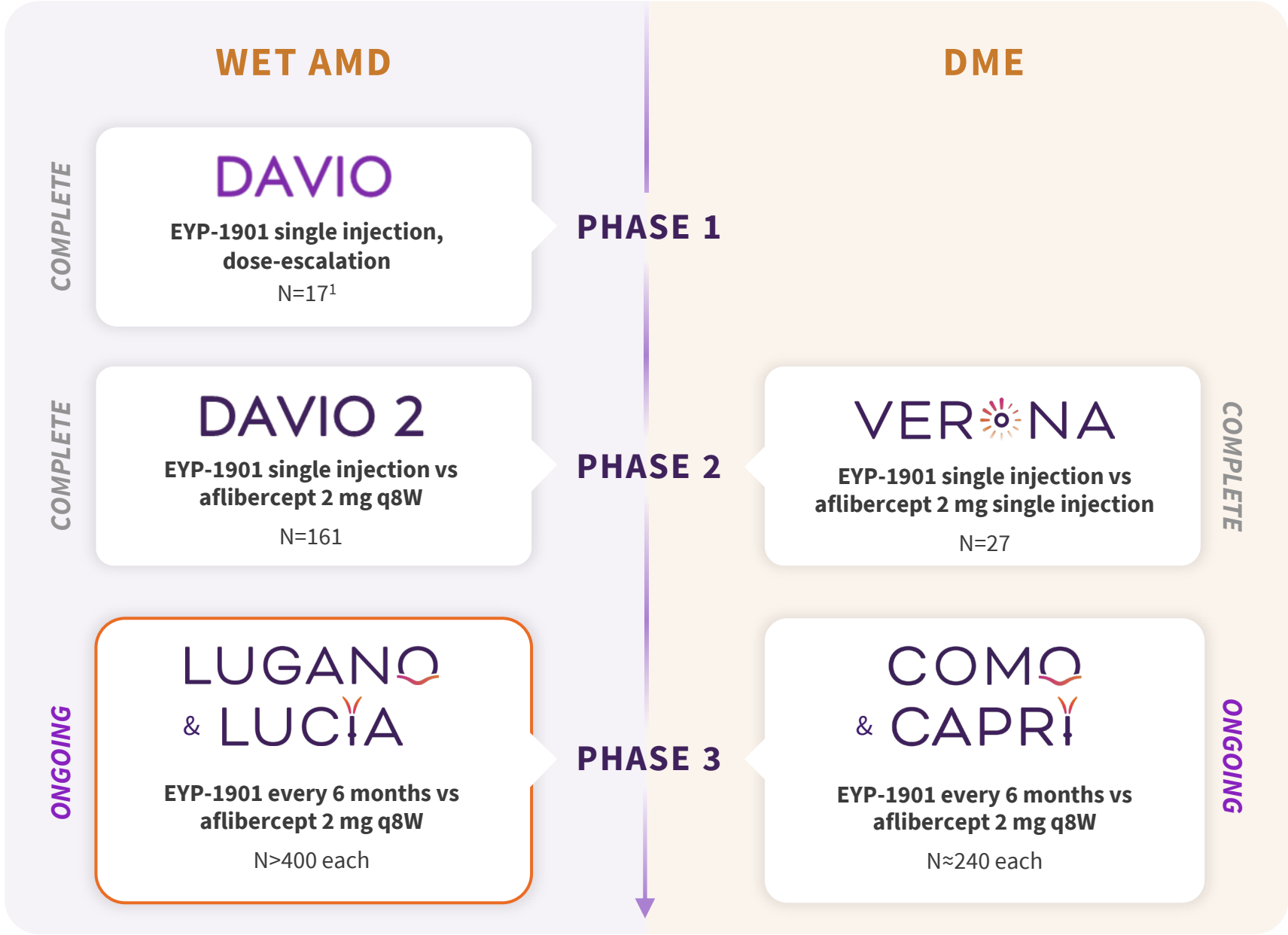
EYP-1901 is an investigational product and its safety and efficacy has not been established. FDA has not approved EYP-1901 in the United States. The materials discussed in this presentation do not predict future FDA approval. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

Clinical Trials of EYP-1901 in Wet AMD and DME

Phase 3 trials in wet AMD and DME fully enrolled and ongoing



1. Patel S, et al. *Ophthalmol Sci.* 2024;4(5):100527.
AMD, age-related macular degeneration; **DME**, diabetic macular edema; **q8W**, every 8 weeks.
Clinicaltrials.gov identifiers: DAVIO NCT04747197; DAVIO 2 NCT05381948; LUGANO NCT06668064; LUCIA NCT06683742; VERONA NCT06099184; COMO NCT07449936; CAPRI NCT07449923.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials

LUGANO and LUCIA: Phase 3 Pivotal Trials Evaluating Noninferiority of EYP-1901 vs On-Label Aflibercept 2 mg in Wet AMD

Objective

Demonstrate that **EYP-1901**, when administered every 6 months, achieves similar visual outcomes to **on-label aflibercept 2 mg** while reducing treatment burden in patients with wet AMD

Primary endpoint

Difference in mean change in BCVA from Day 1 to Weeks 52 and 56 (averaged) vs aflibercept control (NI margin: −4.5 letters)

Secondary endpoints

- **Anatomy**: Change from baseline in CST up to Week 96
- **Supplemental treatment:** Proportion of patients not receiving a supplemental injection of aflibercept up to Week 96
- **Treatment burden:** Annualized rate of injection burden through Week 56
- **Safety:** Incidence and severity of ocular TEAE up to Week 96

Inclusion criteria

- **Previously-treated** *or* **treatment-naïve** patients with a documented diagnosis of wet AMD in the study eye, with disease onset at any time before Screening
- **BCVA between 35 to 78 ETDRS letter score** (≈20/32 to 20/200 Snellen equivalent) in the study eye at Screening and Day 1
- Previously-treated patients must have been treated with **≥2 anti-VEGF IVT injections**[a] in the 6 months prior to Screening

Exclusion criteria

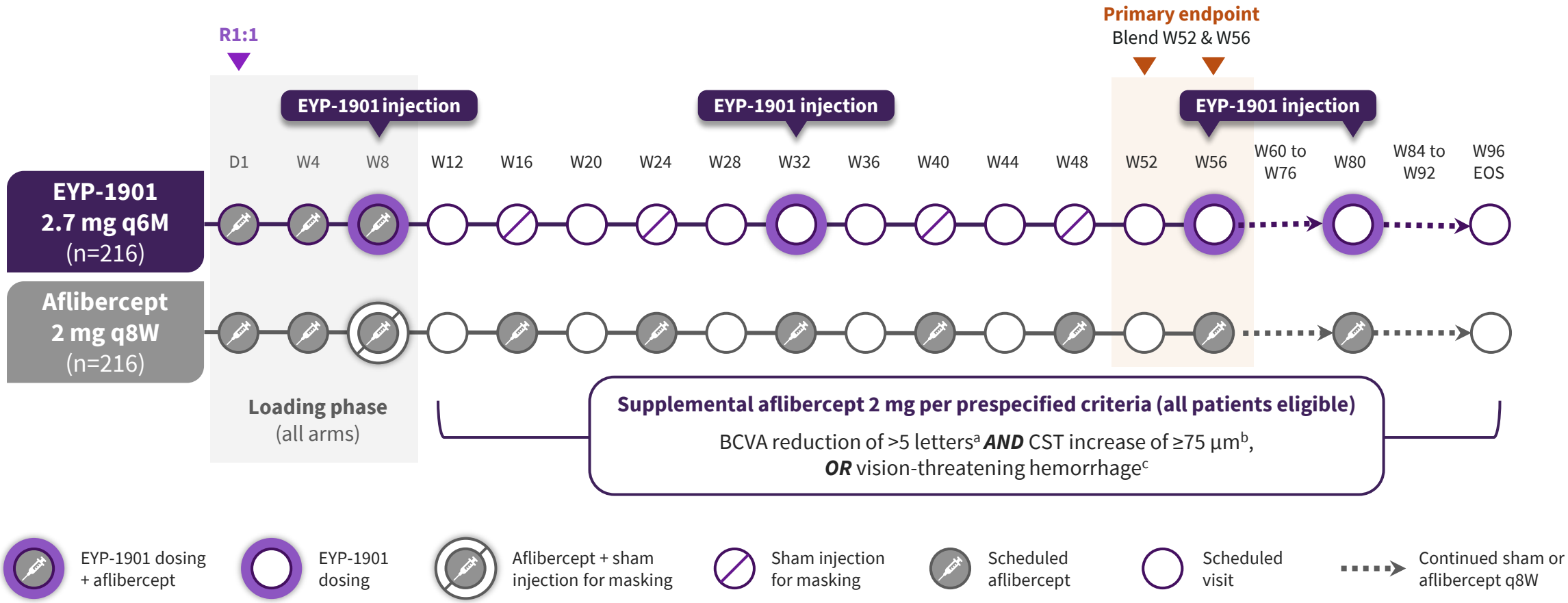
- Subfoveal fibrosis, atrophy, or scarring in the center subfield
- Fellow eye BCVA using ETDRS charts <20 letters (20/400 Snellen equivalent)
- CST >500 µm, RPED >400 µm, retinal pigment epithelial tear
- Uncontrolled ocular hypertension or glaucoma (IOP >25 mmHg or cup to disc ratio ≥0.8)
- Presence of signs indicative of polypoidal choroidal vasculopathy as assessed by the Central Reading Center

The EYP-1901 dose investigated in phase 3 trials is 2.686 mg (two inserts of 1.343 mg each) administered in a single injection. [a]Aflibercept 2 mg, aflibercept 8 mg, bevacizumab (off-label), ranibizumab, or faricimab for wet AMD per standard-of-care in the study eye.
AMD, age-related macular degeneration; **BCVA**, best-corrected visual acuity; **CST**, central subfield thickness; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **IOP**, intraocular pressure; **IVT**, intravitreal; **NI**, noninferiority; **RPED**, retinal pigment epithelial detachment; **TEAE**, treatment-emergent adverse event; **VEGF**, vascular endothelial growth factor. Clinicaltrials.gov identifiers: LUGANO NCT06668064; LUCIA NCT06683742.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

LUGANO: Phase 3 Pivotal Trial Evaluating Noninferiority of EYP-1901 vs On-Label Aflibercept 2 mg in Wet AMD

Patients with treatment-naïve or previously-treated wet AMD



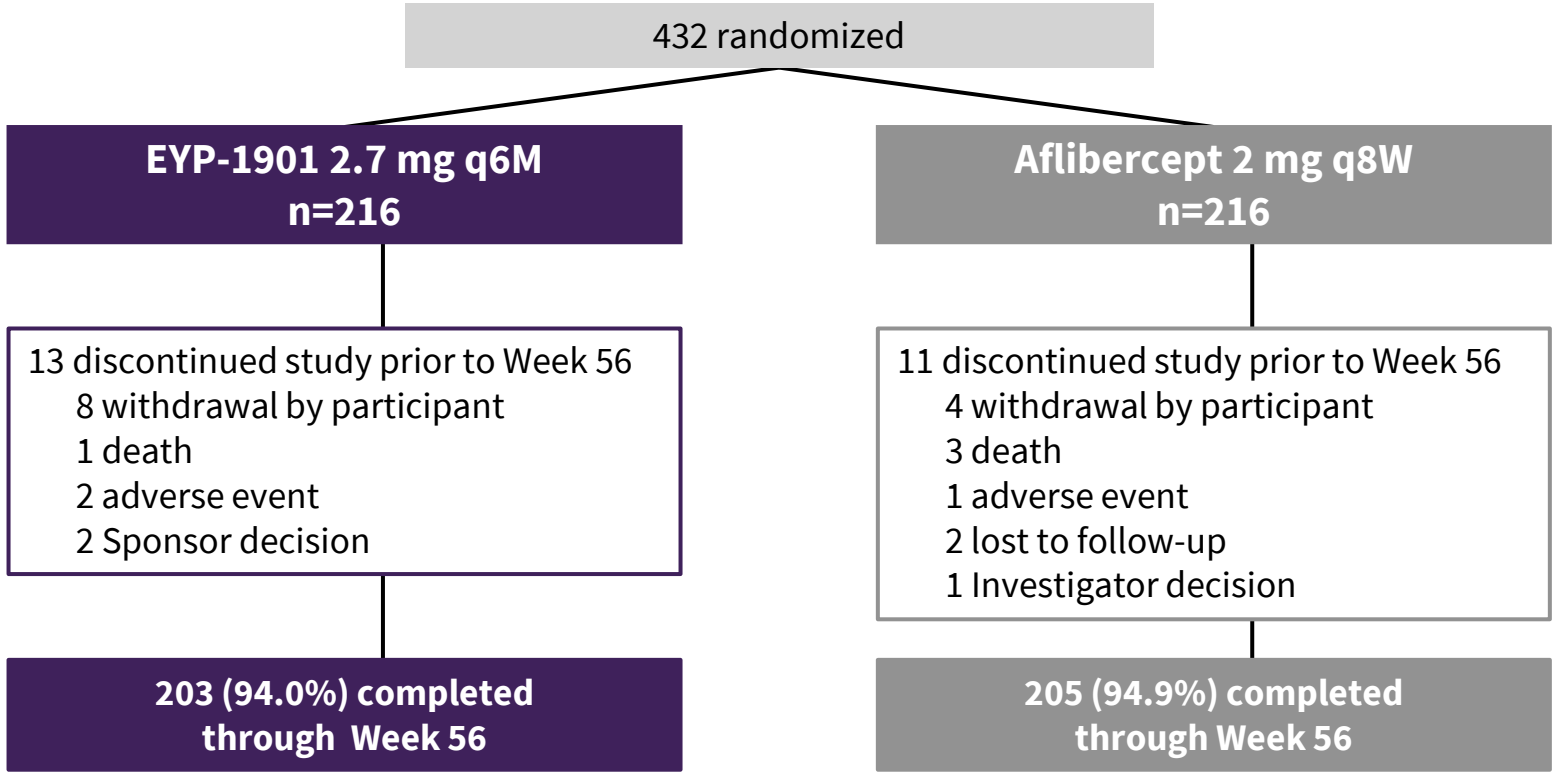
The EYP-1901 dose investigated in phase 3 trials is 2.686 mg (two inserts of 1.343 mg each) administered in a single injection. [a] From best on study measurement due to wet AMD. [b] From lowest on study measurement. Increase in CST must be due to subretinal and/or intraretinal fluid. [c] Requires discussion with supplemental injection monitor.

AMD, age-related macular degeneration; **BCVA**, best-corrected visual acuity; **CST**, central subfield thickness; **D**, day; **EOS**, end of study; **q6M**, every 6 months; **q8W**, every 8 weeks; **R**, randomization; **W**, week.

LUGANO ClinicalTrials.gov identifier: NCT06668064.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

Patient Disposition:
Strong Study Completion and Retention Through Week 56



Low discontinuation rate in both arms (6%)

No study or treatment discontinuation due to EYP-1901

q6M, every 6 months; **q8W**, every 8 weeks. LUGANO Clinicaltrials.gov Identifier: NCT06668064.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

Baseline Characteristics: Well-Balanced Across Treatment Arms

Baseline Characteristics	EYP-1901 2.7 mg q6M (n=211)	Aflibercept 2 mg q8W (n=216)
Age (years), mean (SD)	77.5 (7.52)	77.0 (7.61)
≥ 65, n (%)	202 (95.7)	205 (94.9)
Female, n (%)	136 (64.5)	141 (65.3)
History of anti-VEGF treatment, n (%)		
Treatment naïve, n (%)	159 (75.4)	164 (75.9)
Previously treated, n (%)	52 (24.6)	52 (24.1)
Annualized number of anti-VEGF injections for previously treated patients, mean (SD)	7.35 (2.21)	7.39 (2.01)
BCVA (ETDRS letters), mean (SD)	65.8 (8.95)	64.3 (10.35)
> 65 letters, n (%)	115 (54.5)	116 (53.7)
≤ 65 letters, n (%)	96 (45.5)	100 (46.3)
BCVA categories		
> 69 ETDRS letters (20/40 Snellen equivalent), n (%)	82 (38.9)	79 (36.6)
≤ 69 ETDRS letters (20/40 Snellen equivalent), n (%)	129 (61.1)	137 (63.4)
CST (µm), mean (SD)	319.83 (71.43)	326.01 (71.91)
Total CNV area by FA (mm^2), mean (SD)	5.69 (4.44)	4.60 (3.86)

LUGANO enrolled treatment naïve and previously-treated patients

~320 µm baseline CST

(mean 323 µm; range 147.4-682.9 µm)

~20/50 Snellen equivalent

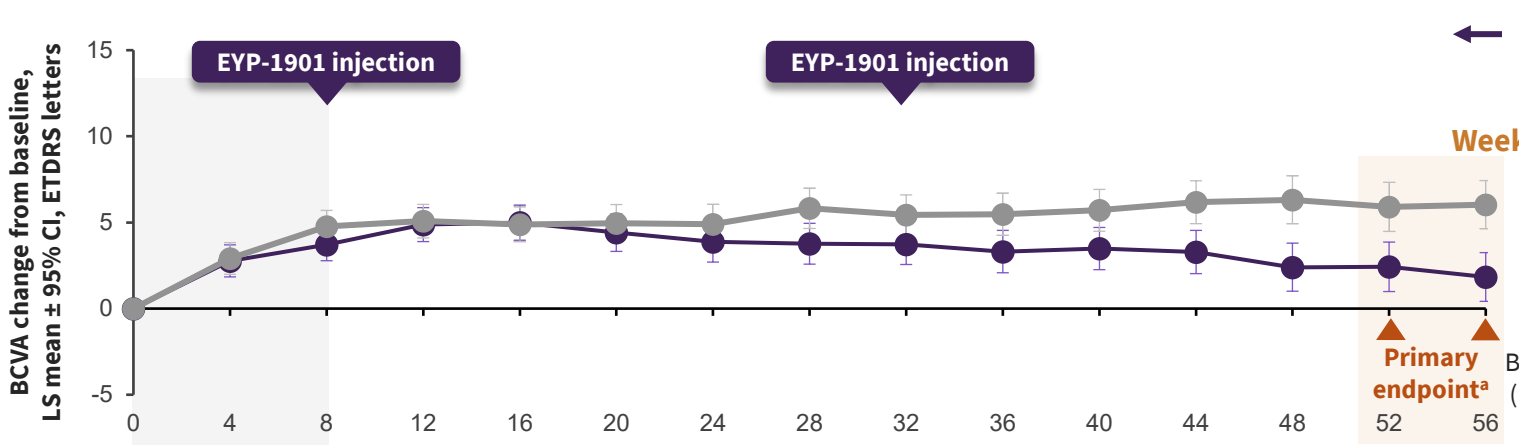
(mean 65.0 ETDRS letters; range 35-79 letters)

Full analysis set. Patients were stratified by baseline BCVA ETDRS score (>65 letters vs ≤65 letters) and history of anti-VEGF therapy for wet AMD (treatment naïve or previously treated). **AMD**, age-related macular degeneration; **BCVA**, best corrected visual acuity; **CNV**, choroidal neovascularization; **CST**, central subfield thickness; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **FA**, fluorescein angiography; **q6M**, every 6 months; **q8W**, every 8 weeks; **VEGF**, vascular endothelial growth factor.
LUGANO Clinicaltrials.gov Identifier: NCT06668064.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

Primary Endpoint Not Achieved in Full Data Set Despite Strong Anatomic Control

Mean BCVA Change from Baseline, Full Analysis Set

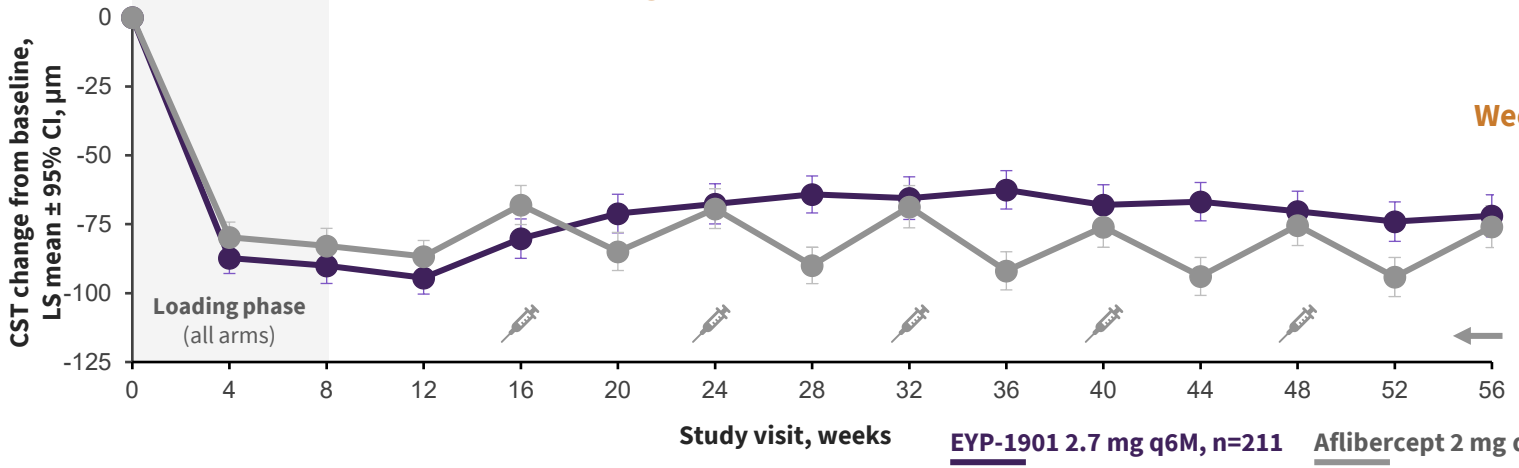


Difference vs aflibercept q8W
−3.84 letters

p=0.2521
95% CI: −5.79, −1.89

BCVA change at Week 52/56 average (Noninferiority margin: −4.5 letters)

Mean CST Change from Baseline, Full Analysis Set



Difference vs aflibercept q8W
+4 µm

[a] Primary endpoint blended Week 52 and Week 56 change from baseline by MMRM.

BCVA, best-corrected visual acuity; **CST**, central subfield thickness; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **LS**, least squares; **MMRM**, mixed model repeated measures; **q6M**, every 6 months; **q8W**, every 8 weeks.

LUGANO Clinicaltrials.gov Identifier: NCT06668064.

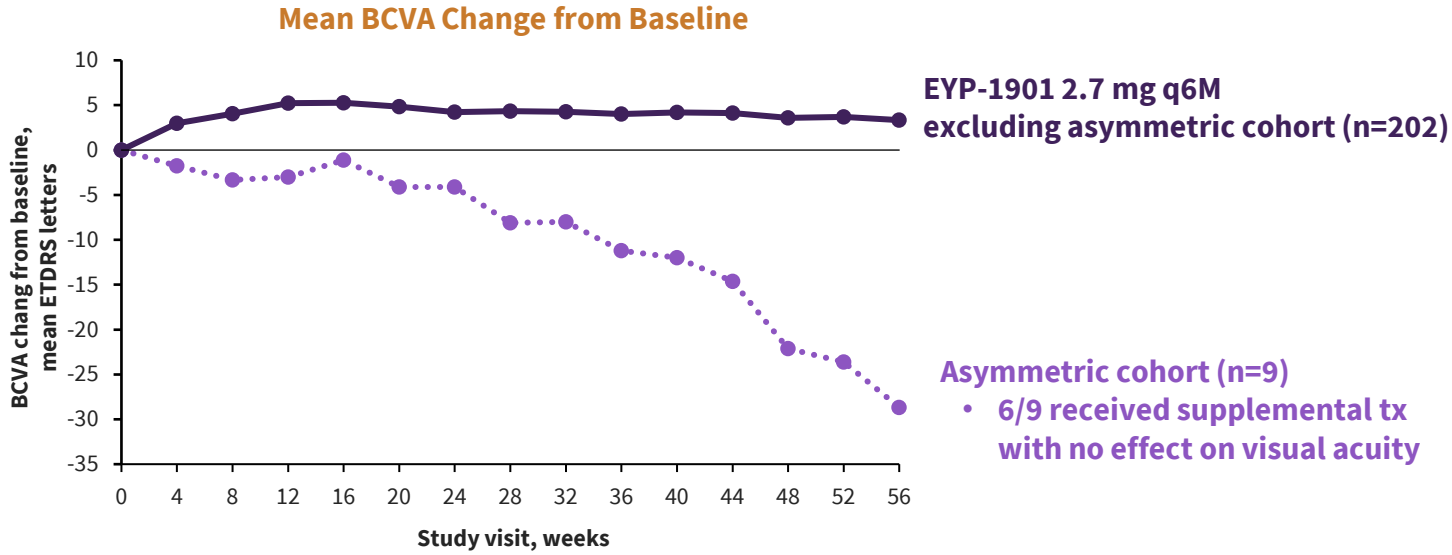
Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

Asymmetric Cohort: Determined to Have Vision Loss Unrelated to Wet AMD

EYP-1901 2.7 mg q6M

9 patients lost ≥15 letters of vision due to non-wet AMD etiologies:

- 6 geographic atrophy
- 2 glaucoma
- 1 retinal detachment



Aflibercept 2 mg q8W

0 patients lost ≥15 letters of vision due to non-wet AMD etiologies

AMD, age-related macular degeneration; **BCVA**, best-corrected visual acuity; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **q6M**, every 6 months; **q8W**, every 8 weeks; **tx**, treatment.
LUGANO Clinicaltrials.gov Identifier: NCT06668064.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

Rates of ≥15 Letter Loss in Previous Wet AMD Trials

	Aflibercept 2 mg q8W		
Trial	**n**	**Timepoint**	**Patients with ≥15 letter loss, %[a]**
VIEW 1	301	Week 52	5.6%[1]
VIEW 2	306	Week 52	4.6%[1]
HAWK	360	Week 48	5.5%[2]
HARRIER	369	Week 48	4.8%[2]
TENAYA	300	Week 40-48, avg	5.9%[3]
LUCERNE	291	Week 40-48, avg	2.7%[3]
DAVIO 2	54	Week 56	7.7%[4]
LUGANO	**216**	**Week 52/56, avg**	**0.5%[4]**

In LUGANO:

1 patient (0.5%) lost ≥15 letters of vision overall

vs

~3-6% in previous trials with aflibercept 2.0 mg q8W

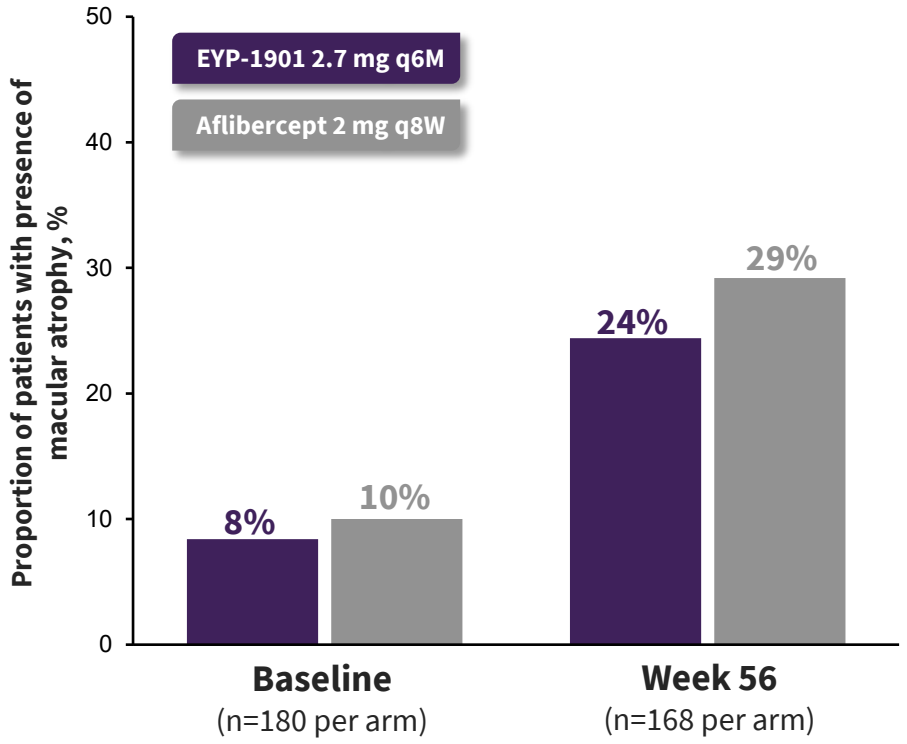
[a] Loss of letters from baseline

1. Heier JS et al *Ophthalmology.* 2012 Dec;119(12):2537-48. **2**. CADTH Common Drug Review: Clinical Review Report for Brolucizumab. 2020. **3**. Heier JS *Lancet.* 2022 Feb 19;399(10326):729-740. **4**. EyePoint data on file.
AMD, age-related macular degeneration; **avg**, average; **q8W**, every 8 weeks.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

No Trend of Worsening GA with EYP-1901 vs Aflibercept 2 mg q8W

GA Presence (by FAF)[a,b]



- **LUGANO excluded patients** with subfoveal fibrosis or atrophy in the **center subfield**
- **Greater new GA** onset in the **aflibercept** arm

GA Growth Rate per IRC

	EYP-1901 Treated Eyes	Untreated Fellow Eye
Eyes with GA at baseline, n	14	30
Growth rate per IRC, mm^2	1.7	1.6

GA growth rate:

- **Consistent** between study eye and fellow eye
- **Slower** than published average of **2.0 mm^2/year**[1-4]

GA Location at Baseline

GA distance from fovea (µm)	EYP-1901 2.7 mg q6M (n=14)	Aflibercept 2 mg q8W (n=17)
At baseline	825	1009
Change from baseline	−236	−254

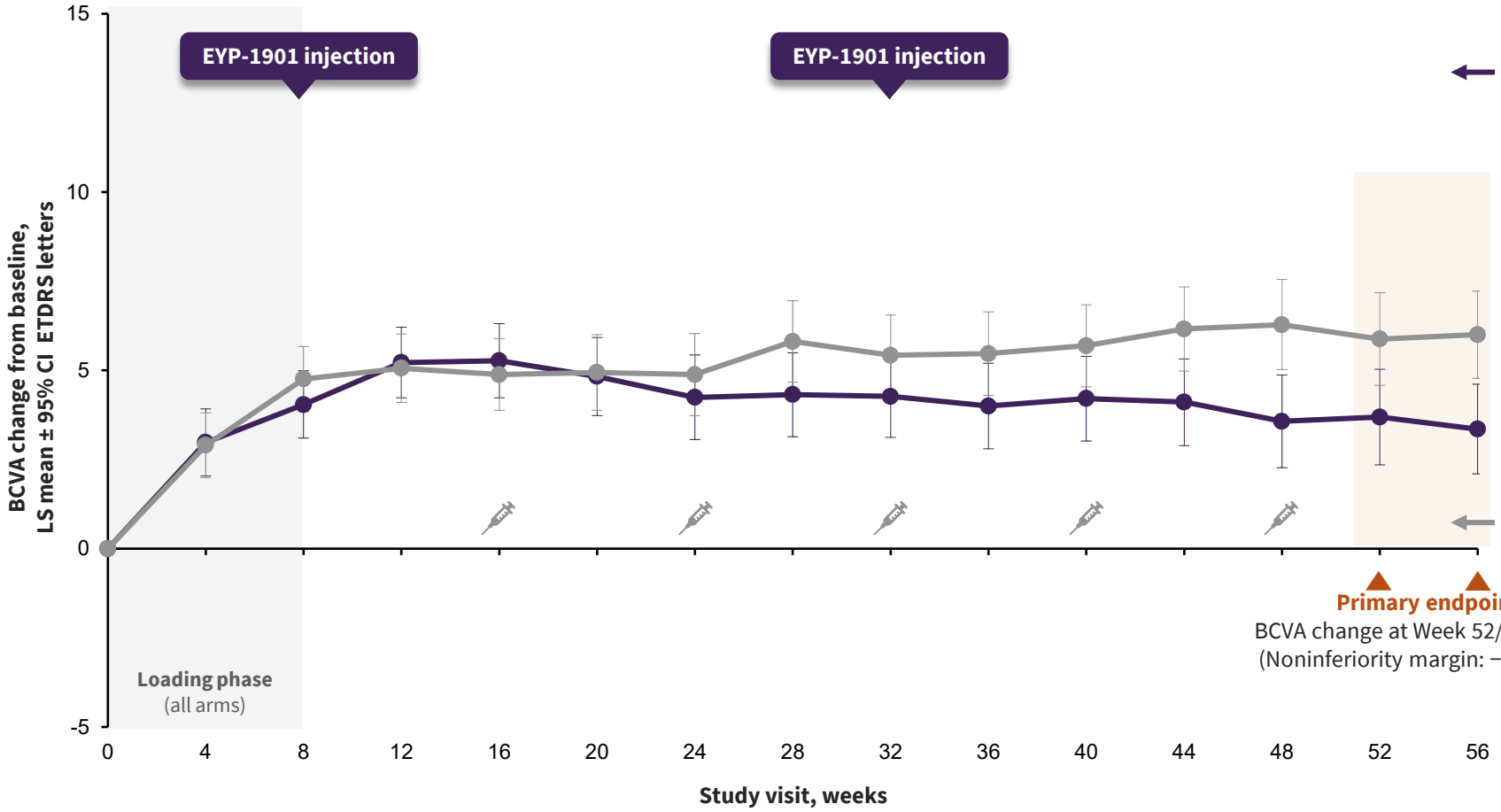
- **GA meaningfully closer to fovea** in EYP-1901 arm versus aflibercept at baseline
- Progression towards fovea was **similar** between groups

[a] GA was measured by FAF. FAF was not a mandatory requirement for the trial. [b] Includes macular atrophy categorized as present or questionable. **1.** Fleckenstein M et al. *Ophthalmology.* 2018 Mar;125(3):369-390. **2.** Holz FG et al. *JAMA Ophthalmol.* 2018 Jun 1;136(6):666-677. **3.** Khanani AK et al. *Lancet.* 2023 Oct 21;402(10411):1449-1458. **4.** Heier JS et al. *Lancet.* 2023 Oct 21;402(10411):1434-1448. **FAF**, fundus autofluorescence; **GA**, geographic atrophy; **IRC**, independent reading center; **q6M,** every 6 months**; q8W**, every 8 weeks.
LUGANO Clinicaltrials.gov Identifier: NCT06668064.

Preliminary data – pending final analysis. Efficacy and safety of EYP-1901 is currently being evaluated in Phase 3 clinical trials.

EYP-1901 Achieved Noninferiority in BCVA Change from Baseline in *Post Hoc* Analysis Excluding Asymmetric Cohort

Mean BCVA Change from Baseline, Asymmetric Cohort (n=9) Excluded



EYP-1901 2.7 mg injections per q6M schedule

Aflibercept 2 mg injections per q8W schedule

Primary endpoint[a]
BCVA change at Week 52/56 average
(Noninferiority margin: −4.5 letters)

BCVA change from baseline, ETDRS letters

	Week 52/56 Average
Aflibercept 2 mg q8W	+5.94
EYP-1901 2.7 mg q6M	**+3.52**

Difference vs aflibercept q8W
−2.42 letters

Nominal p=0.0096
95% CI: −4.16, −0.67

EYP-1901 2.7 mg q6M, n=202

Aflibercept 2 mg q8W, n=216

[a] Primary endpoint blended Week 52 and Week 56 change from baseline by MMRM.

BCVA, best-corrected visual acuity; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **LS**, least squares; **MMRM**, mixed models for repeated measures; **q6M**, every 6 months; **q8W**, every 8 weeks. LUGANO Clinicaltrials.gov Identifier: NCT06668064.

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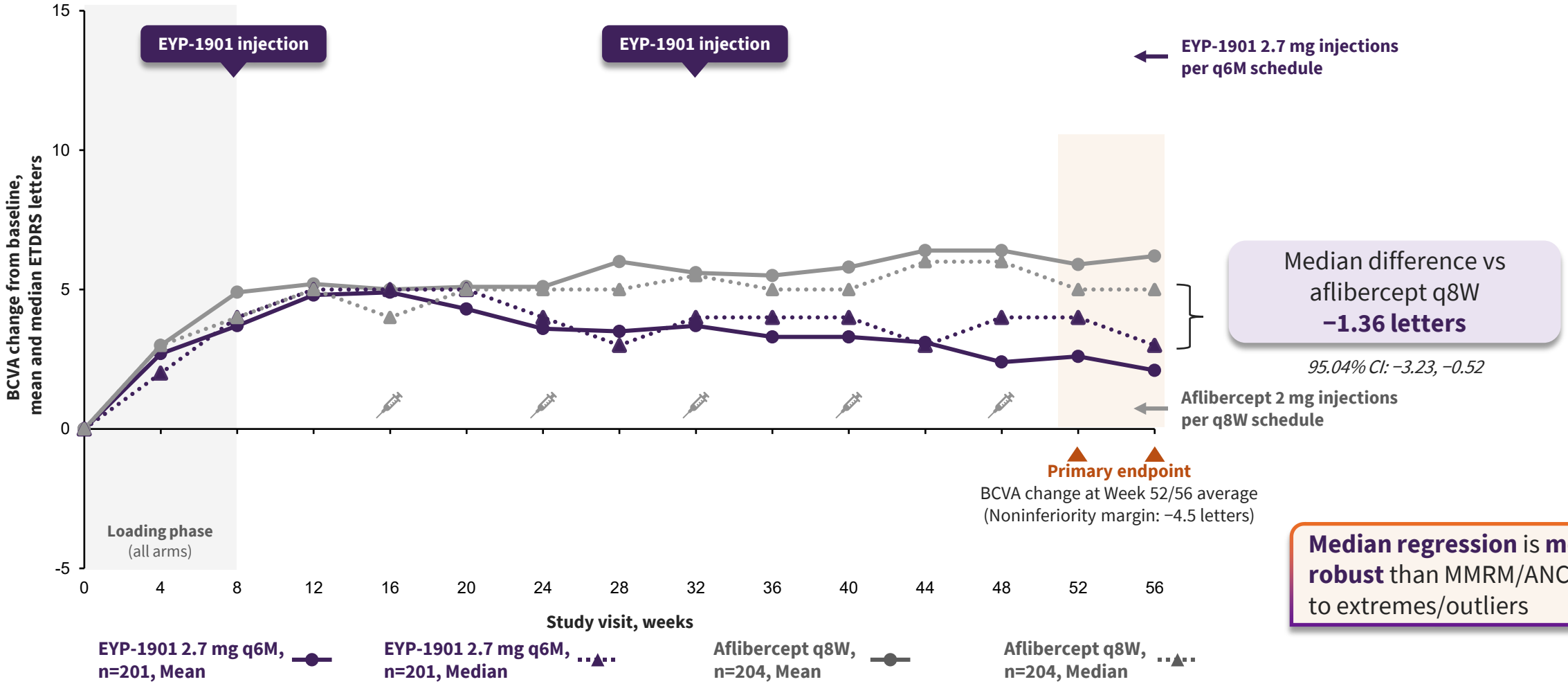
Noninferiority Achieved with Median Regression

Mean and Median BCVA Change from Baseline, Full Analysis Set



Median regression is **more robust** than MMRM/ANCOVA to extremes/outliers

ANCOVA, analysis of covariance; **BCVA**, best-corrected visual acuity; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **MMRM**, mixed models for repeated measures; **q6M**, every 6 months; **q8W**, every 8 weeks.
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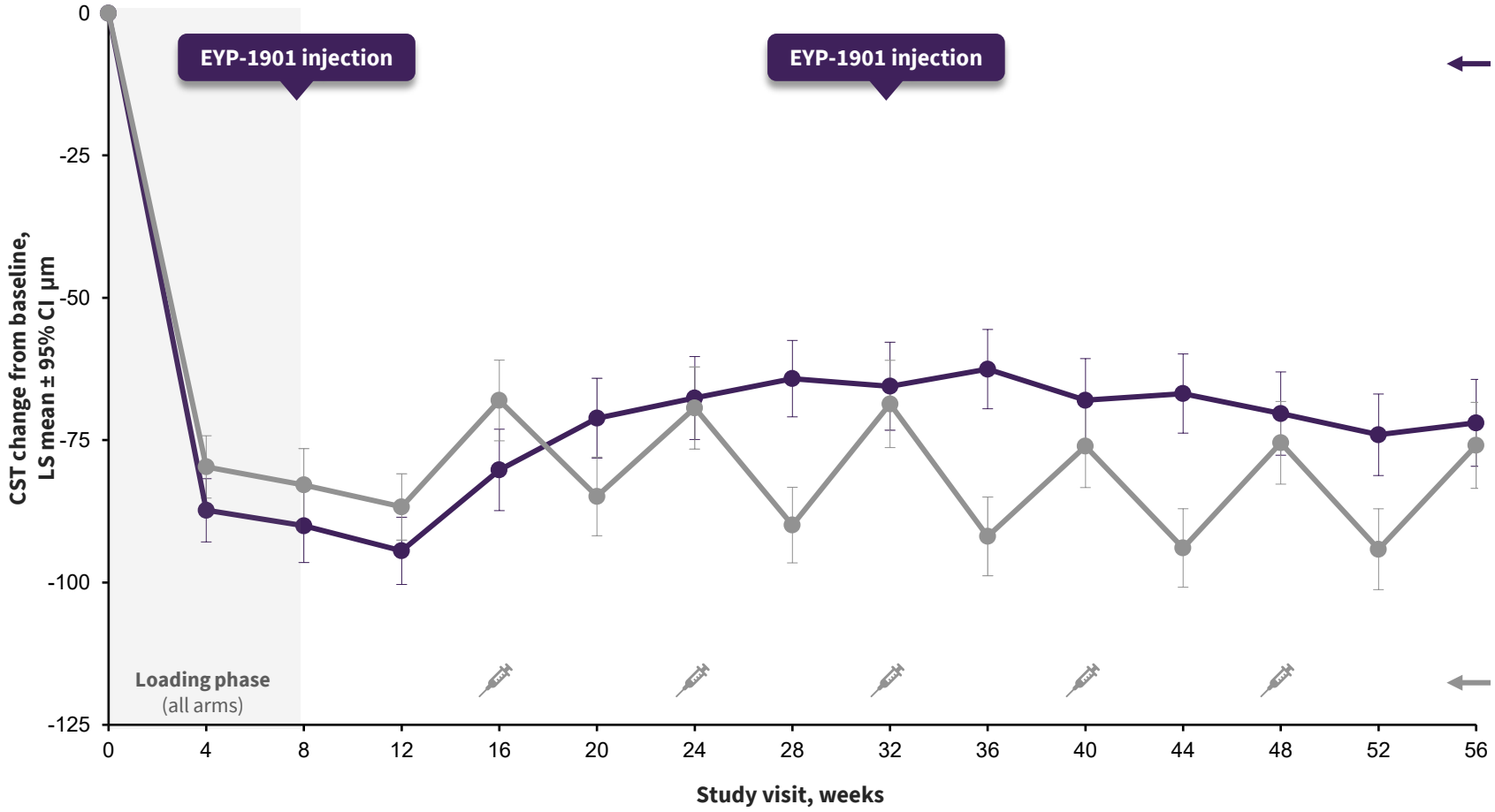
CST Outcomes:
Durable Anatomic Control and No Sawtooth Pattern with EYP-1901

Mean CST Change from Baseline, Full Analysis Set



CST change from baseline, µm	Week 56
EYP-1901 2.7 mg q6M	−72 µm
Aflibercept 2 mg q8W	−76 µm

Difference vs aflibercept q8W **+4 µm**

EYP-1901 2.7 mg q6M, n=211

Aflibercept 2 mg q8W, n=216

CST, central subfield thickness; **LS**, least squares; **q6M**, every 6 months; **q8W**, every 8 weeks. LUGANO Clinicaltrials.gov Identifier: NCT06668064.

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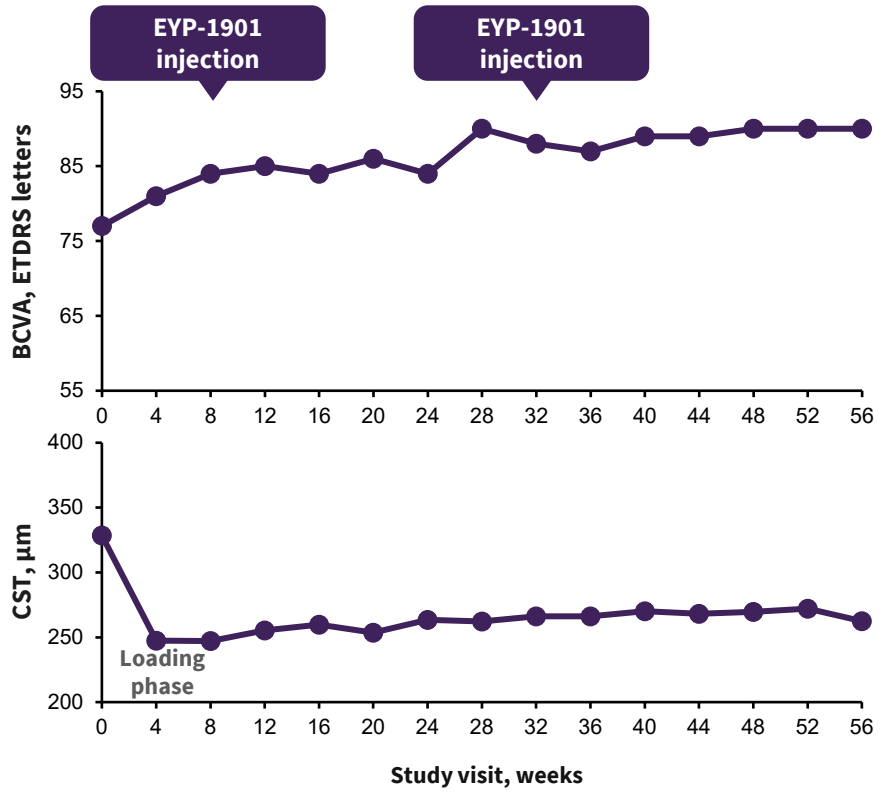
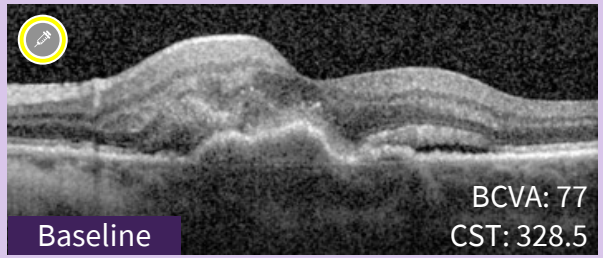
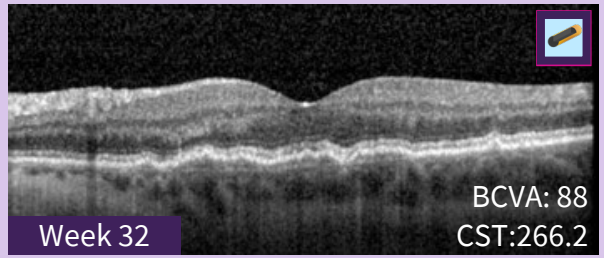
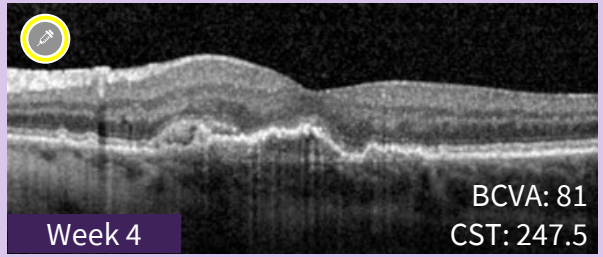
Case Study: EYP-1901 2.7 mg q6M

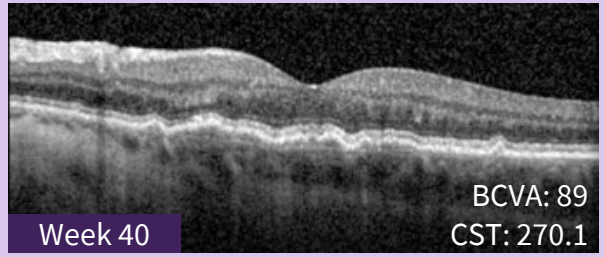
Patient **gained 13 letters** with
EYP-1901 administered every 6 months and
no supplemental treatment

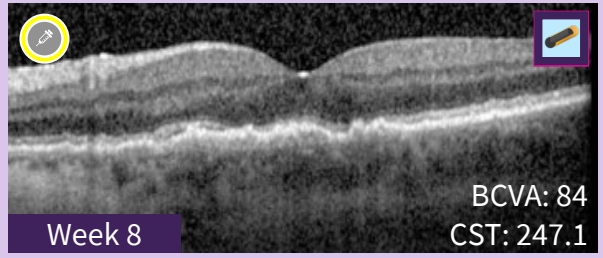


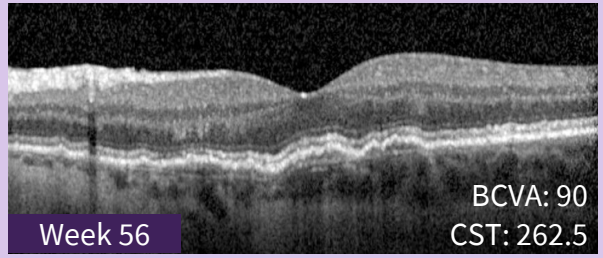


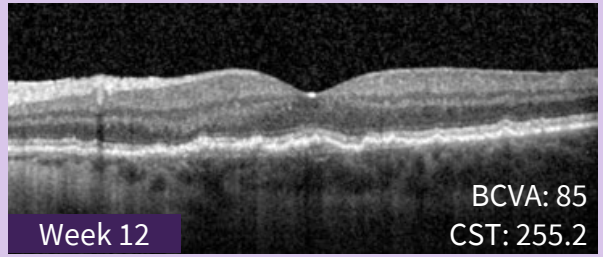












Treatment administration

Aflibercept 2 mg

EYP-1901 2.7 mg

Illustrative patient case; not representative of all observed cases or predicative of treatment outcomes

BCVA, best-corrected visual acuity; **CST**, central subfield thickness; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **q6M**, every 6 months. LUGANO Clinicaltrials.gov Identifier: NCT06668064.

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LUGANO Phase 3 Trial of EYP-1901 2.7 mg q6M versus Aflibercept 2 mg q8W in Wet AMD

- LUGANO **did not demonstrate noninferiority** for mean change from baseline in BCVA in the **full analysis set**
- **Strong anatomic control** observed with EYP-1901 2.7 mg, with only a **+4 µm difference** versus aflibercept q8W at Week 56
- **Noninferior vision outcomes** were achieved with **exclusion of the asymmetric cohort** (9/211 patients) with vision loss of ≥15 letters not due to wet AMD

COMING UP NEXT: TREATMENT BURDEN AND SAFETY RESULTS FROM LUGANO

LUCIA TOPLINE RESULTS EXPECTED Q4 2026

Second pivotal wet AMD trial

AMD, age-related macular degeneration; **BCVA**, best-corrected visual acuity; **q6M**, every 6 months; **q8W**, every 8 weeks. ClinicalTrials.gov identifiers: LUGANO, NCT06668064; LUCIA, NCT06683742.

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