A Study to Evaluate the Efficacy and Safety of Tarcocimab Tedromer and Tabirafusp Tedromer Compared to Aflibercept in Participants with Wet Age-related Macular Degeneration

First-time One-year Primary Efficacy and Safety Outcomes of the Phase 3 DAYBREAK Study

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on behalf of the DAYBREAK Study Group

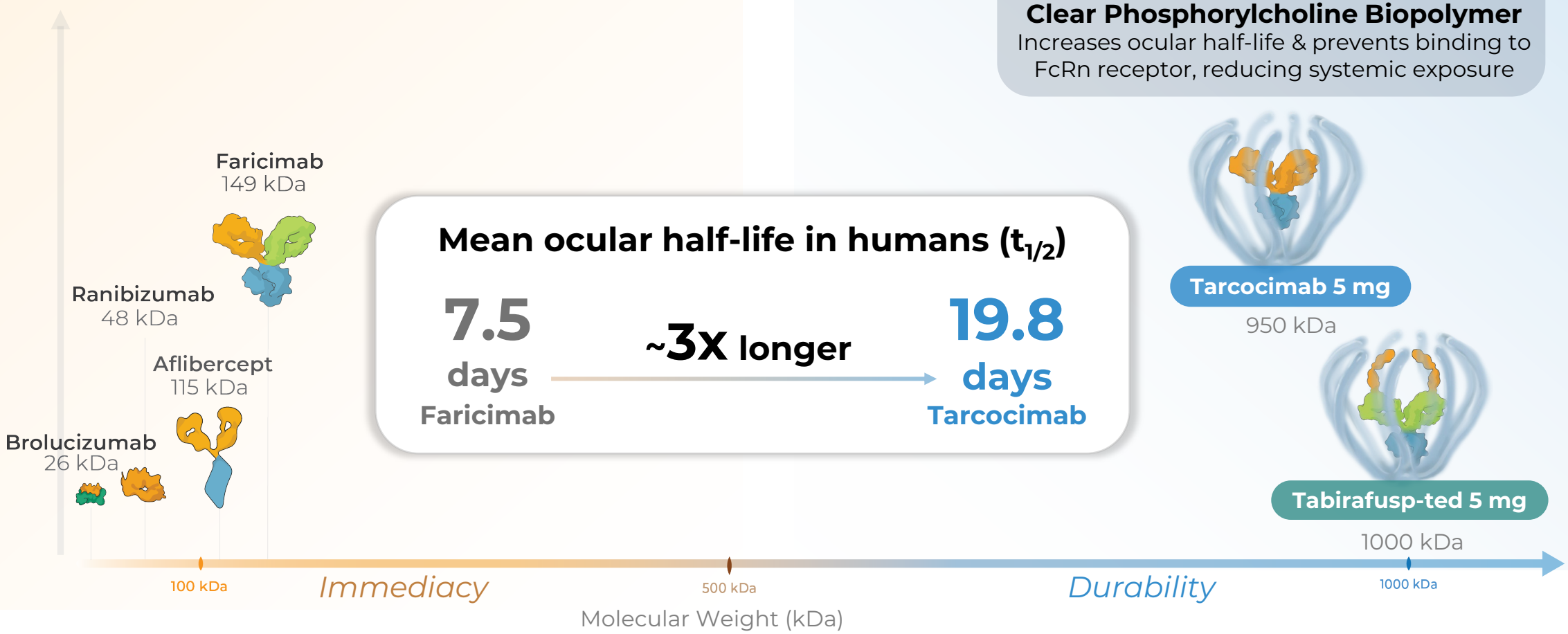
David M. Brown[1]; Robert W. Wong[2]; Margaret Chang[3]; Deepak Sambhara[4]; Scott Fitzpatrick[5]; Dolly Chang[5]; Melina Cavichini Cordeiro[5]; Victor Perlroth[5]; Trinh Pham[5]; Haifeng Zhang[5]; J. Pablo Velazquez-Martin[5]

[1]Retina Consultants of Texas, Houston, US; [2]Austin Retina Associates, Austin, US; [3]Retina Consultants Medical Group, Sacramento, US; [4]Eye Clinic of Wisconsin; [5]Kodiak Sciences, Palo Alto, US.

Website Version

Antibody Biopolymer Conjugate (ABC) medicines leverage high molecular weight to deliver longer ocular durability

Today's anti-VEGF intravitreal biologics



ABC Platform-based medicines*

High Molecular Weight, Optically Clear Phosphorylcholine Biopolymer
Increases ocular half-life & prevents binding to FcRn receptor, reducing systemic exposure

Mean ocular half-life in humans ($t_{1/2}$)

7.5 days Faricimab → **~3x longer** → **19.8 days** Tarcocimab

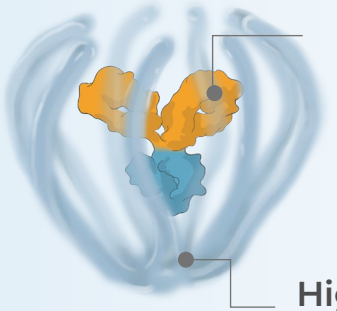
Tarcocimab 5 mg
950 kDa

Tabirafusp-ted 5 mg
1000 kDa

*Conjugated portion shown. ABC medicines tarcocimab and tabirafusp-ted combine conjugated and unconjugated protein in a single intravitreal injection.

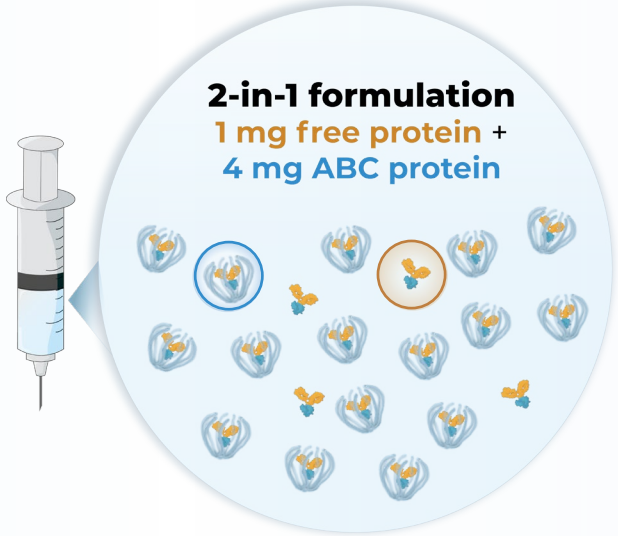
Combining free and conjugated antibodies, ABC medicines are designed to optimize immediacy and durability in a single intravitreal injection

TARCOCIMAB 5 MG

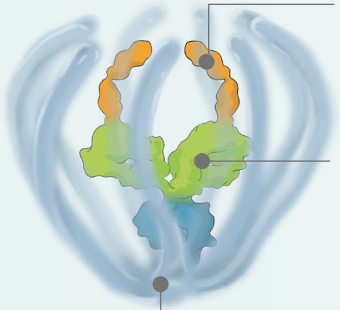


Anti-VEGF antibody

High molecular weight biopolymer



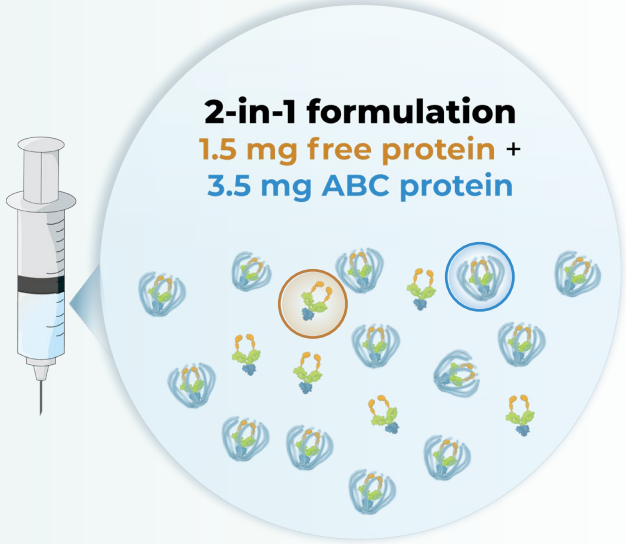
TABIRAFUSP-TED 5 MG



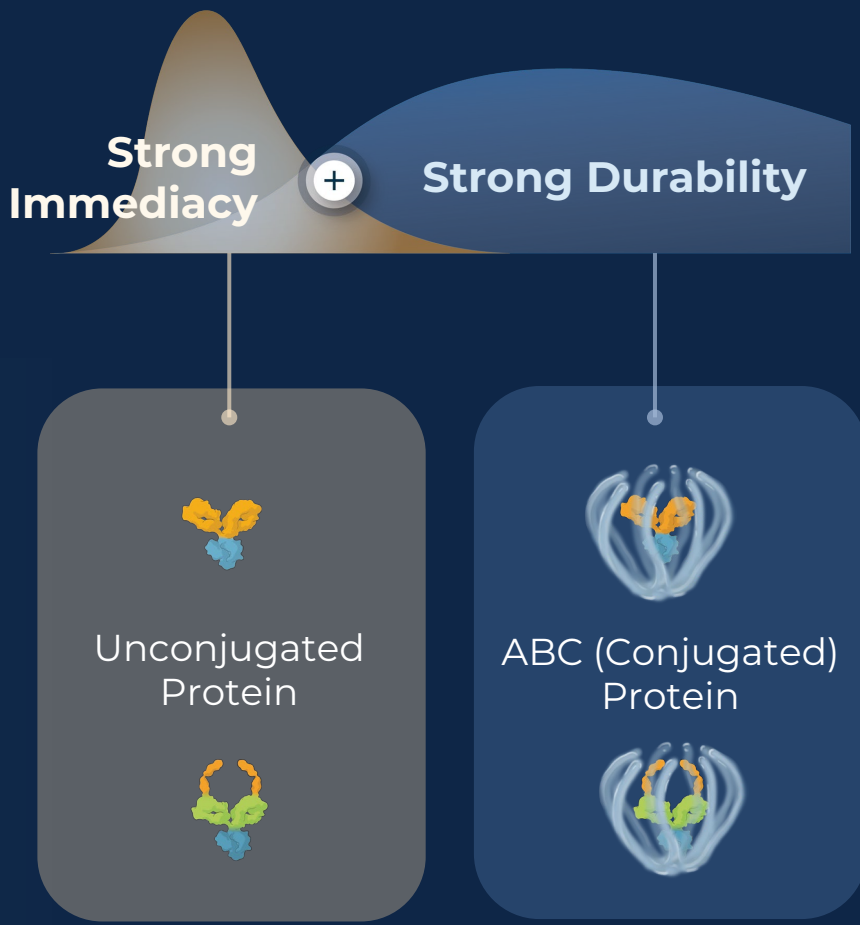
VEGF trap: Broad VEGF inhibition (VEGF-A, VEGF-B, PlGF)

Anti-IL-6 antibody: Potent anti-inflammatory effect; can inhibit up to 2 IL-6 molecules

High molecular weight biopolymer



2-in-1 Formulation



DAYBREAK: Phase 3, double-masked, randomized trial in treatment-naïve wet AMD (n=667)

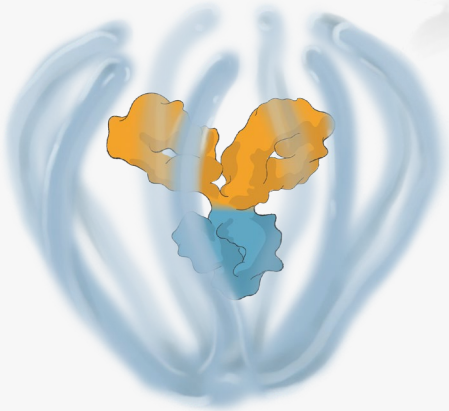
2 molecules independently tested at full alpha vs a single comparator

Single Comparator

Tarcocimab 5 mg	Aflibercept 2 mg	Tabirafusp-ted 5 mg
Extended durability **Individualized 4W – 24W** after 4 monthly loading doses **Objective**: comparable efficacy with up to 6-month dosing	**Per label** **Q8W** after 3 monthly loading doses	**Intensive Dosing** **Q8W + individualized 4W** after 4 monthly loading doses **Objective**: explore efficacy potential with IL-6 and VEGF dual pathway inhibition

Separate pivotal analyses using independent SAPs

NCT06556368. Tarcocimab tedromer also referred to as tarcocimab in this presentation. Tabirafusp tedromer also referred to as tabirafusp-ted in this presentation.
SAP; statistical analysis plan

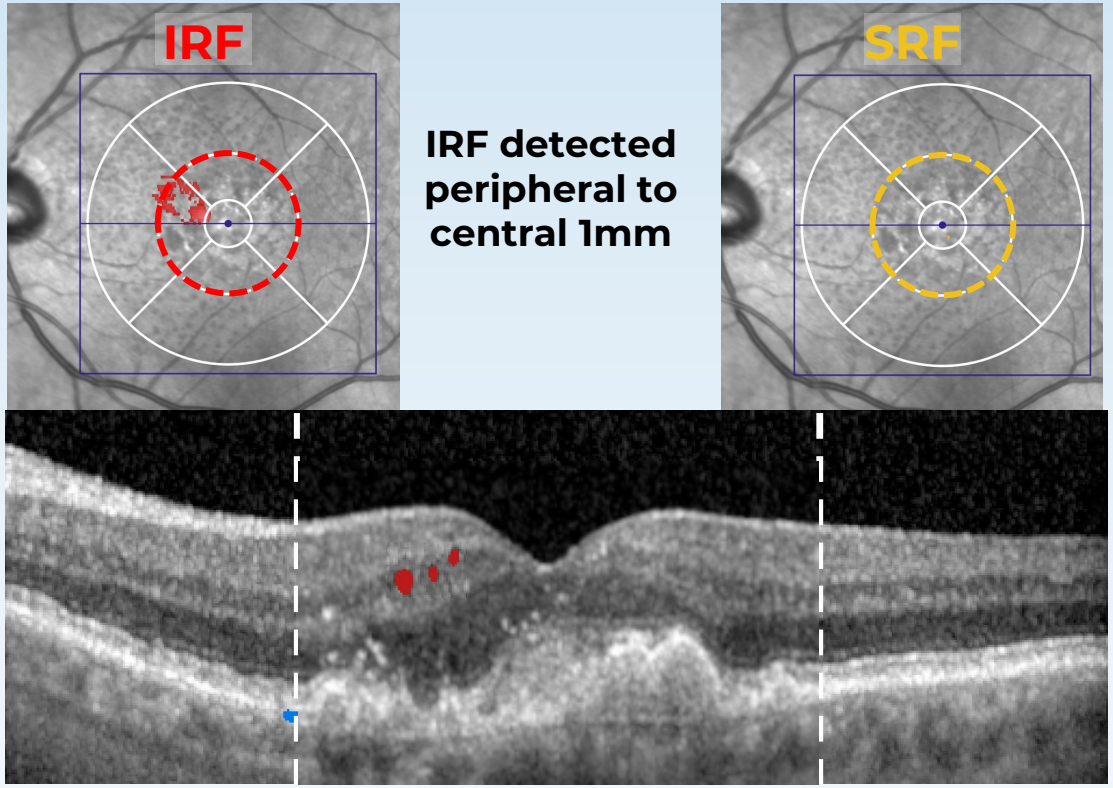


One-year primary efficacy and safety outcomes of the Phase 3 DAYBREAK Study in wet AMD

Efficacy and safety of tarcocimab tedromer compared to aflibercept

An AI-algorithm assessed IRF and SRF presence in the central 3mm to determine retreatment. Real-world decision-making → *Fluid = Treatment*

Central 3 mm has 9-fold the evaluable area of CST (central 1mm)



DAYBREAK disease activity criteria (any of the following)

- Presence of intraretinal fluid (IRF) in central 3mm
- Presence of subretinal fluid (SRF) in central 3mm
- Presence of macular hemorrhage

Goal:

Operationalize how retina specialists determine exudative disease activity using a treat-to-dry approach

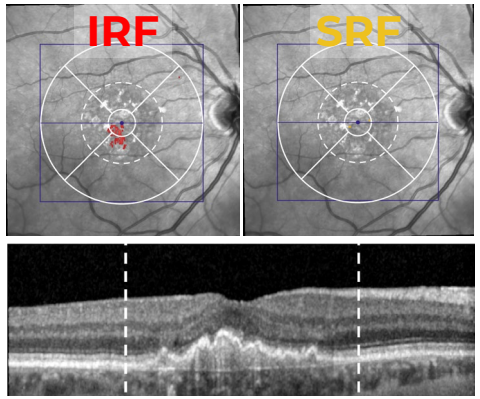
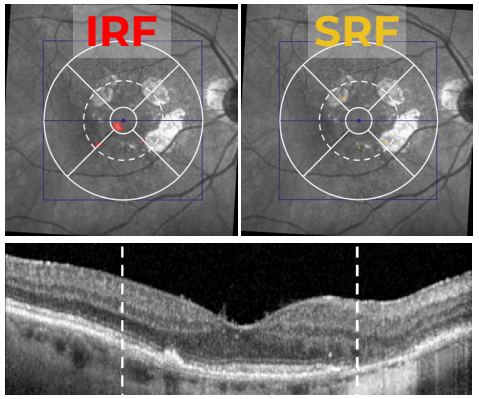
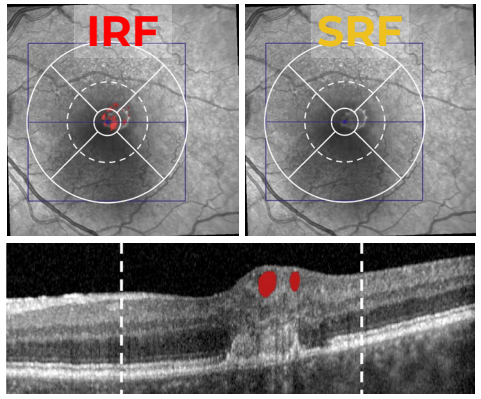
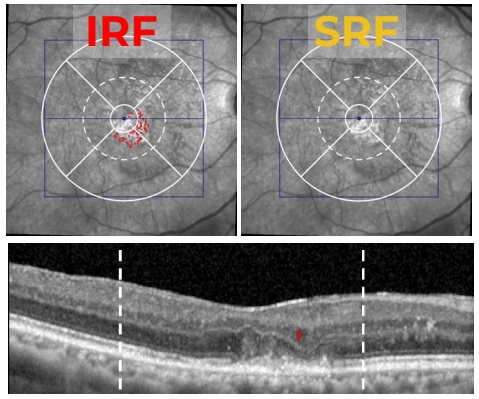
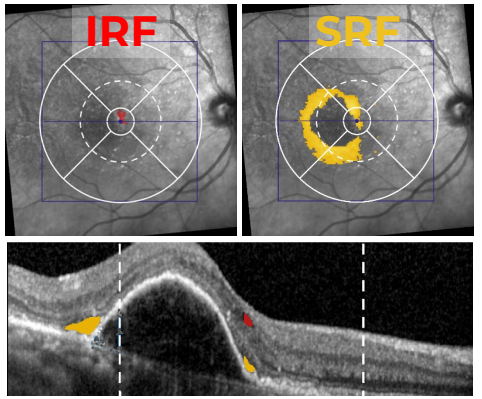
Intentionally NOT required:

Specific CST increase and/or visual acuity loss

DAYBREAK's retreatment criteria strict by design. No undertreatment allowed.

Would these meet disease-activity criteria in any other modern pivotal wAMD trial?

5 different patients: all resulted in re-treatment in DAYBREAK

Case 1	Case 2	Case 3	Case 4	Case 5
				
ΔCST from best[a]: **+32 µm** ΔBCVA from Wk 12[b]: **0**	ΔCST from best[a]: **+16 µm** ΔBCVA from Wk 12[b]: **0**	ΔCST from best[a]: **+3 µm** ΔBCVA from Wk 12[b]: **+3**	ΔCST from best[a]: **+19 µm** ΔBCVA from Wk 12[b]: **+8**	ΔCST from best[a]: **+41 µm** ΔBCVA from Wk 12[b]: **-3**

Would treatment be triggered in different Phase 3 studies?[c]

PULSAR[1]	**No treatment**	**No treatment**	**No treatment**	**No treatment**	**No treatment**
TENAYA & LUCERNE[2]	**No treatment**	**No treatment**	**No treatment**	**No treatment**	**No treatment**
DAYBREAK					

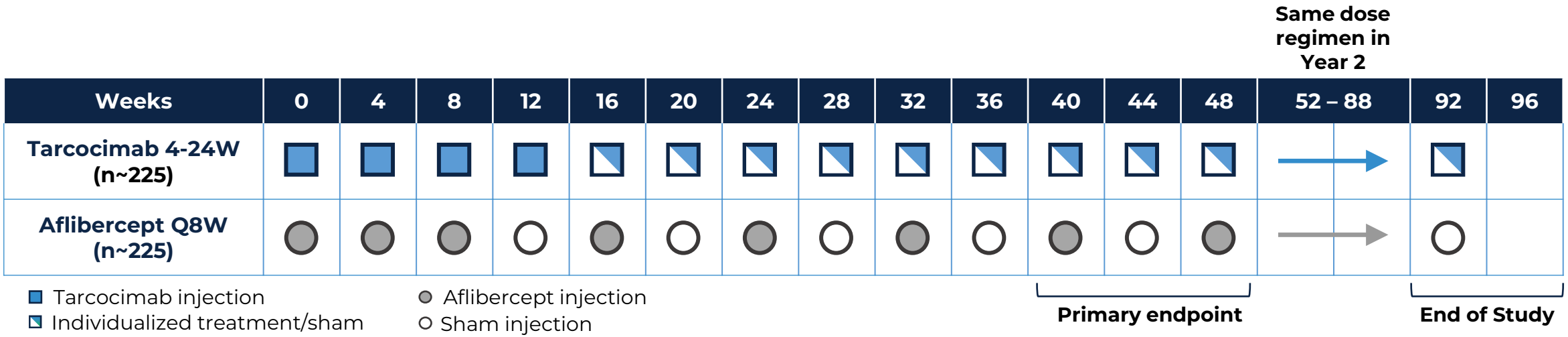
DAYBREAK used strict fluid-based retreatment criteria. Treat-to-dry and maintain dry

a. CST increase measured from best previous CST measurement;
b. BCVA change measured compared to Week 12 value;
c. Refers to treatment decision visits. In TENAYA & LUCERNE, disease activity was assessed at Weeks 20 and 24 and patients were then assigned to fixed Q8W, Q12W, or Q16W dosing through Week 60.

1. Lanzetta, P. et al. *Lancet* (2024) doi:10.1016/S0140-6736(24)00063-1. 2. Khanani, A. M. et al. Ophthalmol Sci 1, (2021).

DAYBREAK – tarcocimab: evaluated the potential for dosing intervals of up to 6 months in wAMD

Tarcocimab



Treatment paradigm

Treat-to-dry with individualized 4W-24W (capped) dosing

Objective

Comparable efficacy with up to 6-month dosing

Primary endpoint

Mean change in BCVA from baseline (Day 1) to the average of Week 40, 44 and 48

wAMD: wet age-related macular degeneration; BCVA: best-corrected visual acuity; Q8W Every 8 weeks

Baseline ocular characteristics were balanced and consistent with treatment-naïve wAMD patients

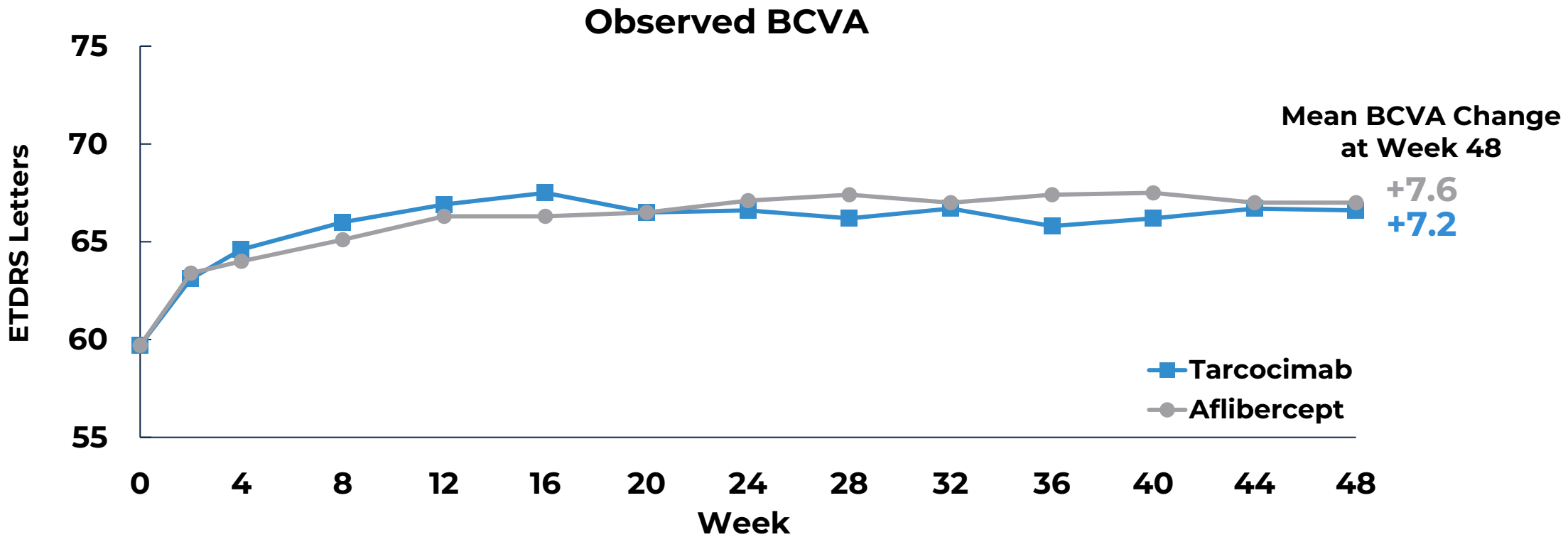
Tarcocimab

	Tarcocimab Q4-24W n= 220	Aflibercept Q8W n= 224
BCVA, ETDRS Letters, mean (SD)	**59.7 (13.48)**	**59.7 (13.29)**
≥20/40 Snellen equivalent, n (%)	72 (32.7%)	72 (32.1%)
≤20/200 Snellen equivalent, n (%)	26 (11.8%)	21 (9.4%)
BCVA Category		
≤ 49 ETDRS Letters, n (%)	44 (20.0%)	43 (19.2%)
50 – 69 ETDRS Letters, n (%)	115 (52.3%)	119 (53.1%)
70 – 78 ETDRS Letters, n (%)	61 (27.7%)	62 (27.7%)
BCVA – Low Luminance VA Difference		
< 33, n (%)	160 (72.7%)	166 (74.1%)
≥ 33, n (%)	59 (26.8%)	58 (25.9%)
OCT Central Subfield Thickness (CST), µm, mean (SD)	**345.8 (113.09)**	**354.9 (108.12)**
Lens Status, n (%)		
Phakic	90 (40.9%)	88 (39.3%)
Pseudophakic	130 (59.1%)	136 (60.7%)
Intraocular Pressure, mmHg, mean (SD)	14.5 (2.90)	14.7 (3.05)

n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm. Snellen equivalent of 20/40 is 69 ETDRS letters and of 20/200 is 38 ETDRS letters.
wAMD: wet age-related macular degeneration; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; VA: visual acuity; OCT: optical coherence tomography

Primary endpoint met: tarcocimab demonstrated meaningful visual gains sustained with up to 6-month dosing

Tarcocimab

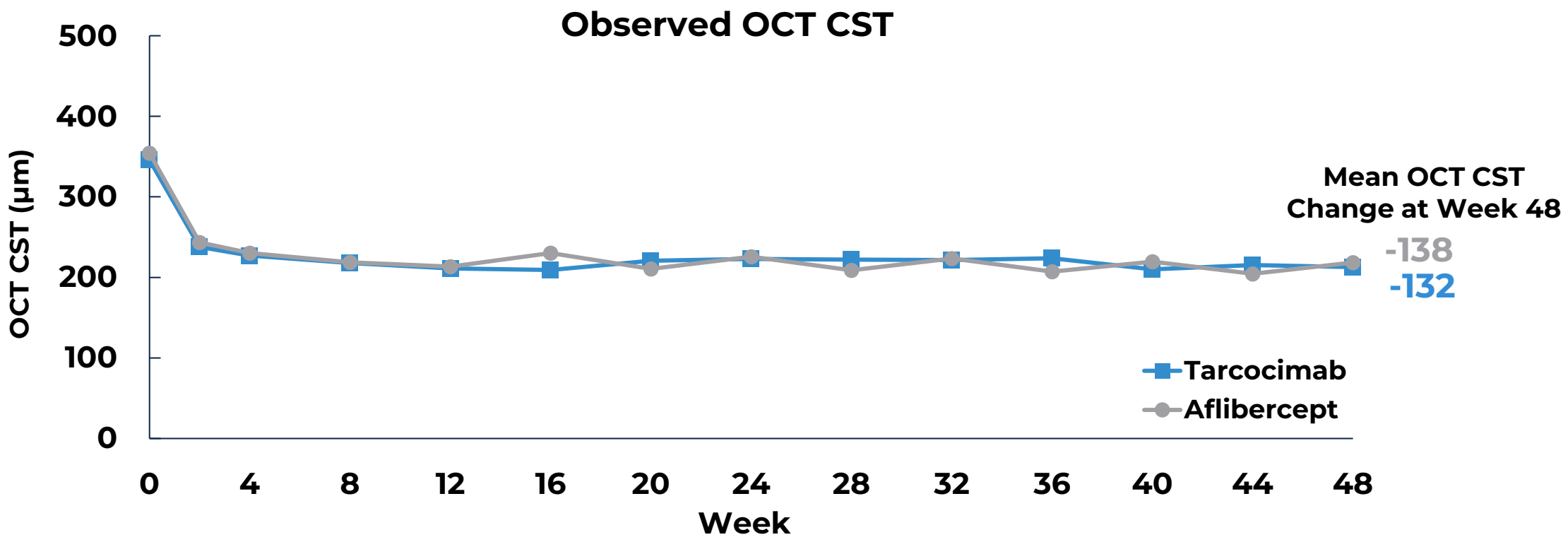


	LSM BCVA change Avg W40-48 (MMRM)[a]	LSM difference[a] (95.02% CI)	***p*-value[a]**
Tarcocimab Q4-24W	6.1	-0.8 (-2.93, 1.32)	**0.0007**
Aflibercept Q8W	6.9		

Observed BCVA and LSM BCVA change (MMRM) analyses use the Full Analysis Set population; tarcocimab n=220; aflibercept n=224.
a. Results for non-inferiority are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 4.5 ETDRS letters
LSM: least square mean; MMRM: mixed model for repeated measures; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study.

Tarcocimab demonstrated rapid and sustained retinal drying in extended dosing with intervals up to 6-months

Tarcocimab



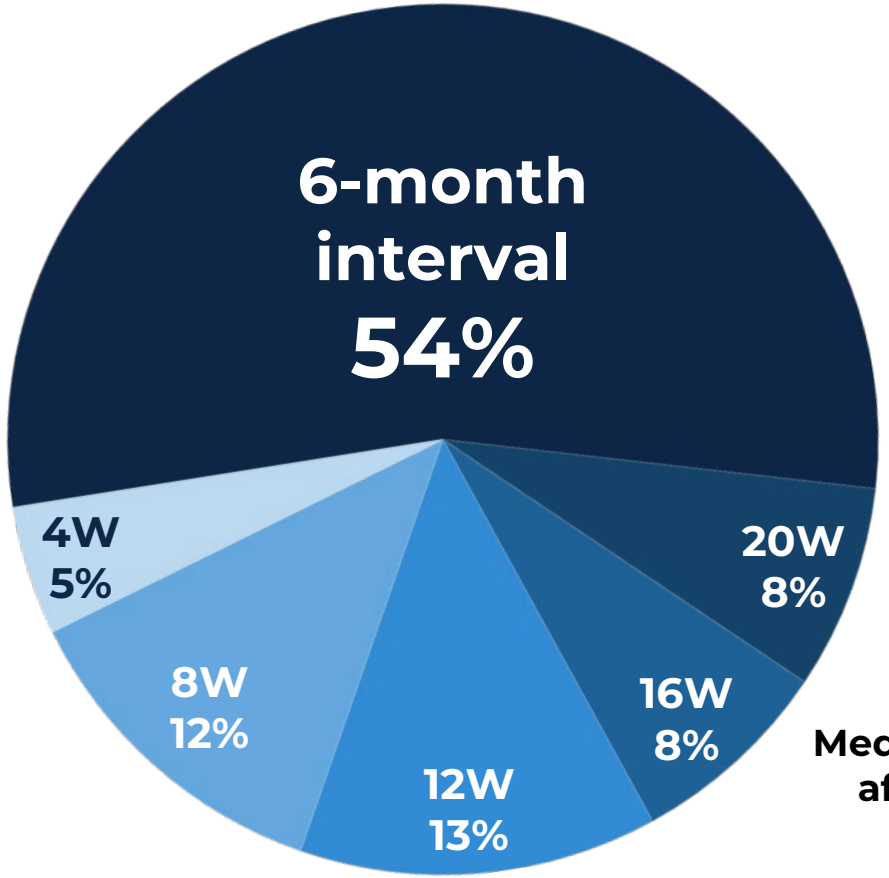
	LSM OCT CST change at W48 (MMRM)[a]	LSM difference[a] (95.02% CI)	**Nominal *p*-value[a]**
Tarcocimab Q4-24W	-139.3	-5.8 (-17.52, 5.90)	**<0.0001**
Aflibercept Q8W	-133.5		

Observed OCT CST and LSM OCT CST change (MMRM) analyses use the Full Analysis Set population; tarcocimab n=220; aflibercept n=224
a. Nominal p-value as not prespecified for hypothesis testing. Results for non-inferiority are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 75 microns.
LSM: least square mean; OCT: optical coherence tomography; CST: central subfield thickness.

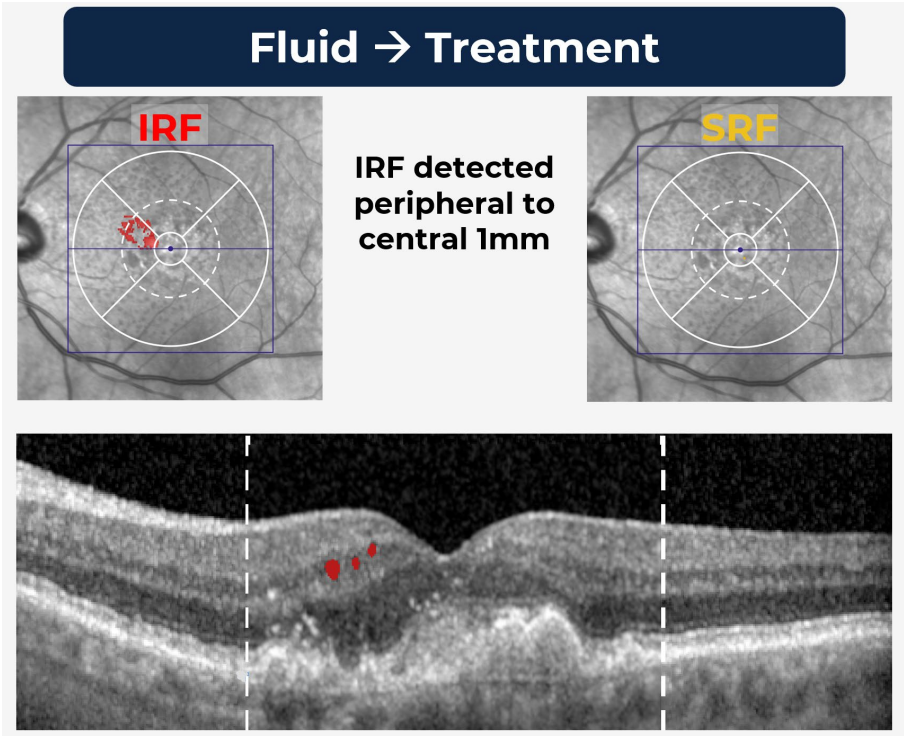
Durability: using real-world retreatment criteria, more than half of tarcocimab patients achieved 6-month dosing

Tarcocimab

Interval at the Primary Endpoint[a]



YEAR 1
Median number of injections after the loading phase[b]
Tarcocimab – 1
Aflibercept – 5



48% of patients achieved a 6-month interval immediately after the loading phase

Strict Treat-to-Dry & Maintain Dry Real-world Durability

a. Prespecified durability analysis includes tarcocimab patients with any completed visit on or after Week 36 (n=210).
b. Number of injections from Week 16 through Week 48 (tarcocimab n=220; aflibercept n=224)
IRF: Intraretinal fluid; SRF: Subretinal fluid; 4W, 4-week interval; 8W, 8-week interval; 12W, 12-week interval; 16W, 16-week interval; 20W, 20-week interval

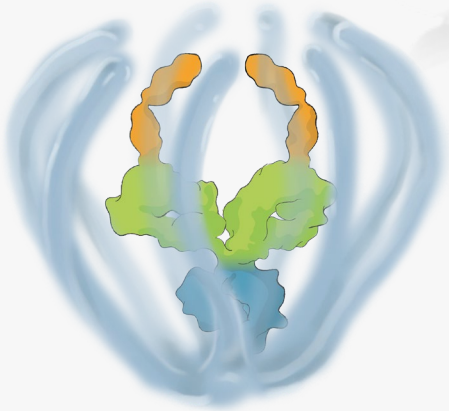
Tarcocimab was well-tolerated

Tarcocimab

Ocular Adverse Events (AEs) up to Week 48	Tarcocimab n = 220	Aflibercept n = 224
Subjects with any AE in the Study Eye, n (%)[a]		
Subjects with ≥1 AEs	89 (40.5%)	79 (35.3%)
Serious AEs	2 (0.9%)	1 (0.4%)
AEs leading to treatment discontinuation	1 (0.5%)	3 (1.3%)
Selected AEs in the Study Eye, n (%)[b]		
Retinal hemorrhage	9 (4.1%)	12 (5.4%)
Eye Pain	8 (3.6%)	5 (2.2%)
Elevated IOP	2 (0.9%)	2 (0.9%)
Retinal pigment epithelial tear	2 (0.9%)	2 (0.9%)
Cataract[c]	1 (0.5%)	2 (0.9%)
Intraocular inflammation	0	0
Occlusive retinal vasculitis	0	0
Endophthalmitis	0	0

Results presented for the Safety Analysis Set. Events are investigator reported. Treatment emergent adverse events. Includes AEs with start date ≥first study drug date up to the Week 48 primary endpoint visit. For participants who discontinued study treatment, AEs include events up until 28 days after the last dose of study intervention (active or sham).

a. Includes all adverse events (AE) reported. A single patient can have multiple events of the same AE term reported and can be counted in different AE terms.
b. Total number of patients with one or more adverse event. A patient with multiple events of the same AE term reported are only counted once.
c. Includes the following cataract AE terms: cataract, cataract cortical, cataract nuclear, posterior subcapsular cataract and lenticular opacities.

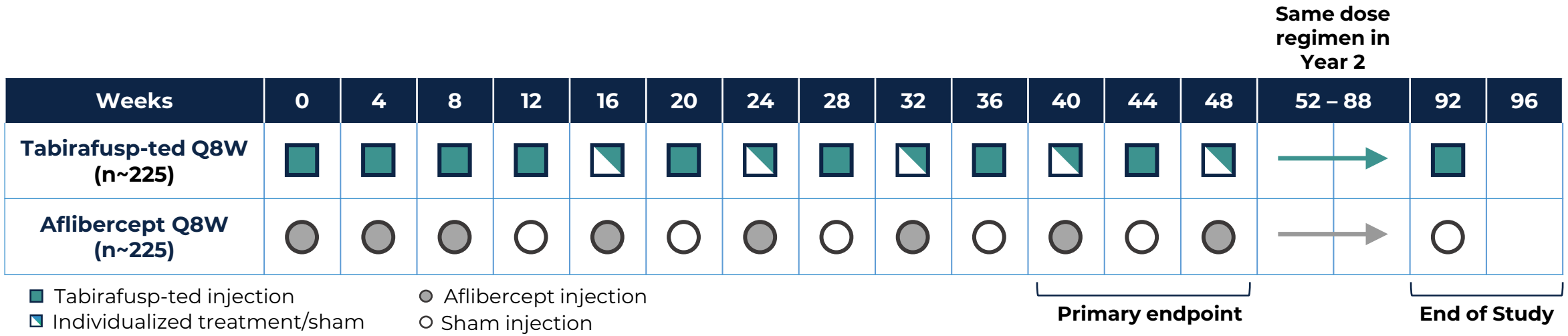


One-year primary efficacy and safety outcomes of the Phase 3 DAYBREAK Study in Wet AMD

Efficacy and safety of tabirafusp alfa tedromer compared to aflibercept

DAYBREAK – tabirafusp-ted: explored if dual VEGF and IL-6 inhibition can improve outcomes in treatment-naïve wAMD

Tabirafusp-ted



Treatment paradigm

Proactive bi-monthly dosing, with individualized monthly doses

Objective

Explore efficacy potential with dual VEGF and IL-6 inhibition in treatment-naïve wAMD

Primary endpoint

Mean change in BCVA from baseline (Day 1) to the average of Week 40, 44 and 48

IL-6: interleukin-6; Q8W: every 8 weeks; VEGF: vascular endothelial growth factor; wAMD: wet age-related macular degeneration; BCVA: best corrected visual acuity.

Baseline ocular characteristics were balanced and consistent with treatment-naïve wAMD patients

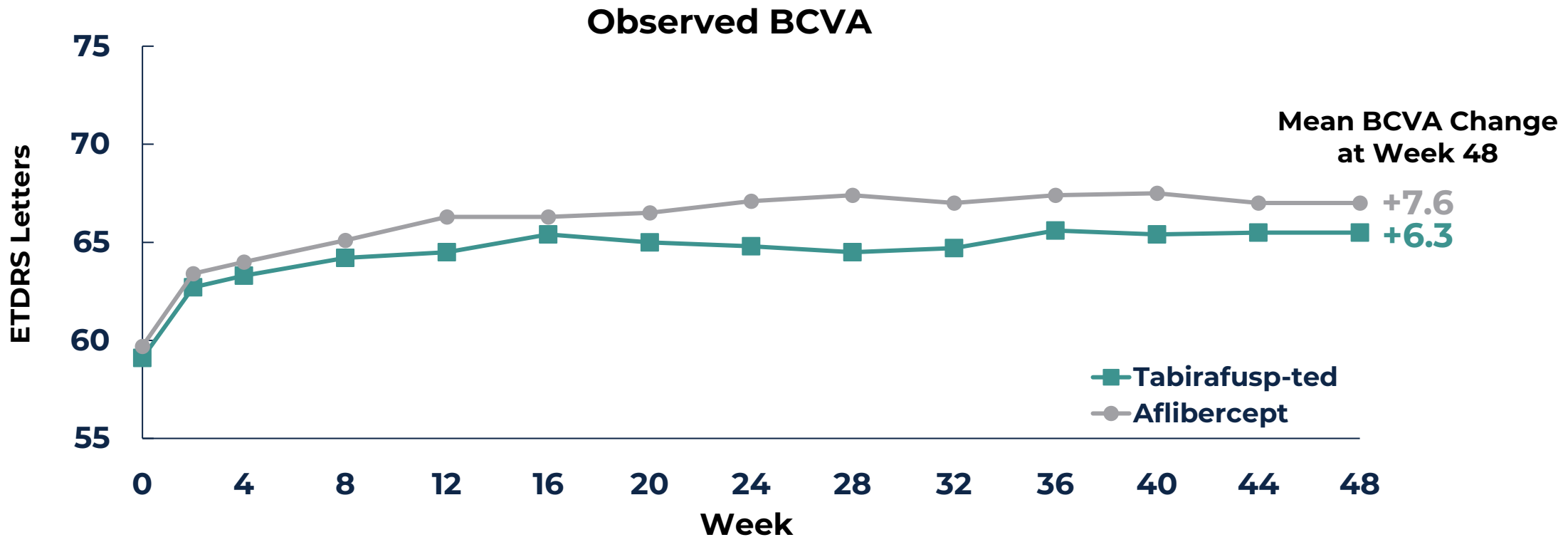
Tabirafusp-ted

	Tabirafusp-ted Q8W n=223	Aflibercept Q8W n= 224
BCVA, ETDRS Letters, mean (SD)	**59.1 (13.54)**	**59.7 (13.29)**
≥20/40 Snellen equivalent, n (%)	73 (32.7%)	72 (32.1%)
≤20/200 Snellen equivalent, n (%)	25 (11.2%)	21 (9.4%)
BCVA Category		
≤ 49 ETDRS Letters	45 (20.2%)	43 (19.2%)
50 – 69 ETDRS Letters	114 (51.1%)	119 (53.1%)
70 – 78 ETDRS Letters	64 (28.7%)	62 (27.7%)
BCVA – Low Luminance VA Difference		
< 33, n (%)	164 (73.5%)	166 (74.1%)
≥ 33, n (%)	59 (26.5%)	58 (25.9%)
OCT Central Subfield Thickness (CST), µm, mean (SD)	**357.0 (114.22)**	**354.9 (108.12)**
Lens Status, n (%)		
Phakic	90 (40.4%)	88 (39.3%)
Pseudophakic	133 (59.6%)	136 (60.7%)
Intraocular Pressure, mmHg, mean (SD)	14.9 (3.30)	14.7 (3.05)

n = Number of participants treated; The denominator for percentages is the number of participants treated within each treatment arm. Snellen equivalent of 20/40 is 69 ETDRS letters and of 20/200 is 38 ETDRS letters. wAMD: wet age-related macular degeneration; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; VA: visual acuity; OCT: optical coherence tomography

Primary endpoint met: tabirafusp-ted demonstrated meaningful visual gains

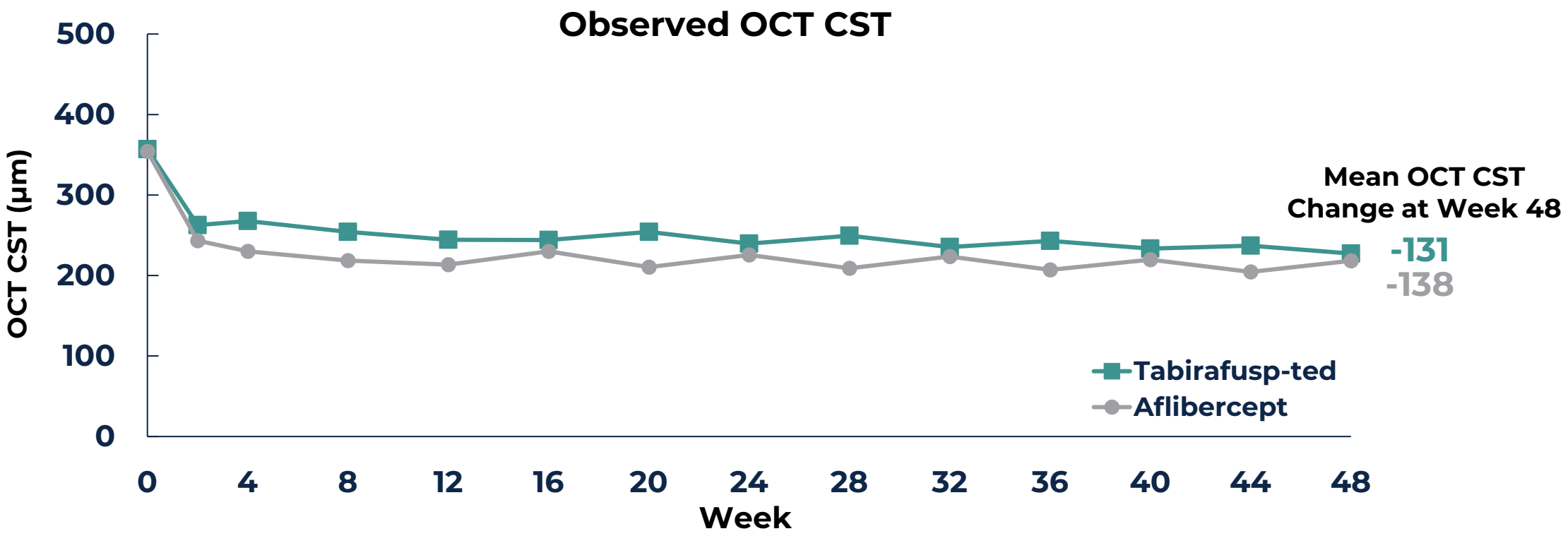
Tabirafusp-ted



	LSM BCVA change Avg W40-48 (MMRM)[a]	LSM difference [a] (95.02% CI)	***p*-value[a]**
Tabirafusp-ted Q8W	5.3	-1.3 (-3.45, 0.87)	**0.0036**
Aflibercept Q8W	6.6		

Observed BCVA and LSM BCVA change (MMRM) analyses use the Full Analysis Set population; tabirafusp-ted n=223; aflibercept n=224
a. Results for non-inferiority are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 4.5 ETDRS letters
LSM: least square mean; MMRM: mixed model for repeated measures; BCVA: best-corrected visual acuity; ETDRS: early treatment diabetic retinopathy study; Q8W: every 8 weeks.

Tabirafusp-ted achieved non-inferior retinal drying compared to aflibercept



	LSM OCT CST change at W48 (MMRM)[a]	LSM difference [a] (95.02% CI)	*p*-value[a]
Tabirafusp-ted Q8W	-132.3	6.6 (-6.22 , 19.35)	**<0.0001**
Aflibercept Q8W	-138.8		

Observed OCT CST and LSM OCT CST change (MMRM) analyses use the Full Analysis Set population; tabirafusp-ted n=223; aflibercept n=224
a. Results are based on a MMRM model including the change from baseline value as the dependent variable. Non-inferiority margin = 75 microns.
OCT: optical coherence tomography; CST: central subfield thickness; Q8W: every 8 weeks.

Tabirafusp-ted was well-tolerated

Ocular Adverse Events (AEs) up to Week 48	Tabirafusp-ted n = 223	Aflibercept n = 224
Subjects with any AE in the Study Eye, n (%)[a]		
Subjects with ≥1 AEs	85 (38.1%)	79 (35.3%)
Serious AEs	0	1 (0.4%)
AEs leading to treatment discontinuation	1 (0.4%)	3 (1.3%)
Selected AEs in the Study Eye, n (%)[b]		
Retinal hemorrhage	15 (6.7%)	12 (5.4%)
Retinal pigment epithelial tear	1 (0.4%)	2 (0.9%)
Intraocular inflammation	1 (0.4%)	0
Eye Pain	0	5 (2.2%)
Elevated IOP	0	2 (0.9%)
Cataract[c]	0	2 (0.9%)
Occlusive retinal vasculitis	0	0
Endophthalmitis	0	0

Results presented for the Safety Analysis Set. Events are investigator reported. Treatment emergent adverse events. Includes AEs with start date ≥first study drug date up to the Week 48 primary endpoint visit. For participants who discontinued study treatment, AEs include events up until 28 days after the last dose of study intervention (active or sham).

a. Includes all adverse events (AE) reported. A single patient can have multiple events of the same AE term reported and can be counted in different AE terms.
b. Total number of patients with one or more adverse event. A patient with multiple events of the same AE term reported are only counted once.
c. Includes the following cataract AE terms: cataract, cataract cortical, cataract nuclear, posterior subcapsular cataract and lenticular opacities.

Tarcocimab & tabirafusp-ted met their independent primary endpoints in DAYBREAK: Equivalence in BCVA compared to Q8W aflibercept

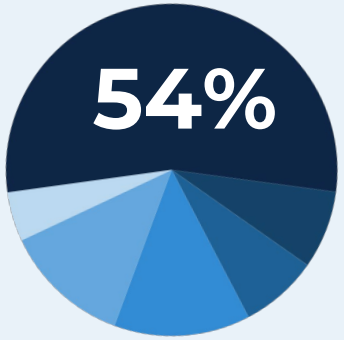
Tarcocimab



Strong vision gains
Noninferior vs aflibercept Q8W (p=0.0007)

Rapid and sustained reduction in CST
Maintained through Week 48 (nominal p<0.0001)

New benchmark in durability

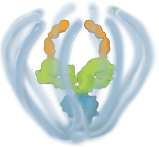


6-month durability

At the primary endpoint, using a strict fluid-based retreatment criteria

Multi-indication BLA in wAMD, DR and RVO on track for submission in 2026

Tabirafusp-ted



Equivalent vision gains
Versus aflibercept Q8W (p=0.0036)

Equivalent retinal drying
Versus aflibercept Q8W (p<0.0001)

Exploring additional benefits

Planned post hoc analyses will evaluate which specific subgroups of wAMD patients may have added benefit from dual VEGF and IL-6 inhibition

Phase 3 ALTO study is actively enrolling in DME, a disease in which IL-6 driven inflammation plays an important role

With DAYBREAK, tarcocimab has completed 5 positive Phase 3 studies across three indications and is BLA-ready

Wet AMD

DAYBREAK DAYLIGHT

- 54% of patients on **6-month dosing**
- Rapid and sustained disease control
- Monthly dosing enabled

Diabetic Retinopathy

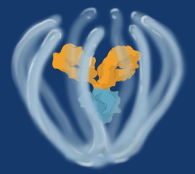
GLOW1 GLOW2

- 100% of patients on **6-month dosing**
- Proliferative disease and mild DME included in trial
- Dosing flexibility

Retinal Vein Occlusion

BEACON

- 75% of patients on **6-month dosing**[1]
- Doubled treatment interval (Q8W) at 6 months



Setting a new standard of care in durability

Multi-indication BLA submission in 2026

BLA: biologics license application
1. Durability interval calculated based on patients that received no injections (46%) or 1 injection (29%) over the second 6 months of Year 1.